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| 28120 | 7590 | 04/18/2011 | EXAMINER | |
| ROPE & GRAY LLP IPRM - Floor 43 PRUDENTIAL TOWER 800 BOYLSTON STREET BOSTON, MA 02199-3600 | | | GAMBEL, PHILLIP | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPatentMail@ropesgray.com
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Office Action Summary

Application No.

10/655,861

Applicant(s)

WANG, YI

Examiner

PHILLIP GAMBEL

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1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 January 2011.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11, 15-18, 20-21, 45-51, 59 and 60 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11, 15-18, 20-21, 45-51 and 59-60 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-946)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Applicant's amendment, filed 01/25/2011, has been entered.

Claims 1-9, 15, 20-21 and 51 have been amended.

Claims 59-60 have been added.

Claims 12-14 and 52-58 have been canceled.
Claims 19 and 22-44 have been canceled previously.

Claims 1-11, 15-18, 20-21, 45-51 and 59-60 are pending.

Applicant's election without traverse of Group I, drawn to methods of treating asthma with anti-C5 antibodies, filed 11/13/2006, has been acknowledged (e.g., see Office Action, mailed 03/13/2007).

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Office Action will be in response to applicant's arguments, filed 01/25/2011.

The rejections of record can be found in the previous Office Action, mailed 10/25/2010.

Upon reconsideration of applicant's arguments, filed 01/25/2011, particularly as it applies to the teachings of Krause, including its disclosure of anti-C5 antibodies as a C5a receptor-inactive therapeutic agent;

New Grounds of Rejection under 35 U.S.C. 103(a) obviousness have been set forth herein for clarity.

While applicant relies upon the disclosure of paragraphs [0206]-[0207] of Krause et al. to stand for the prior art anti-C5 antibodies to be C5a receptor-inactive therapeutic agents, the following is noted.

In contrast to applicant's assertions, paragraph [0207] of Krause describes anti-C5 antibodies such as eculizumab or pexelizumab, which are the same anti-C5 antibodies based upon the anti-C5 antibody 5G1.1 recited in the instant claim and encompassed by anti-C5 antibodies that inhibit the conversion of C5 into C5a and C5b.

Ecuzumab is the humanized version of the anti-C5 antibody, 5G1.1

Pexelizumab is the humanized single chain version of the anti-C5 antibody, 5G1.1.

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[0206] Still other embodiments of the invention are directed to combinations in which at least one C5a receptor-inactive therapeutic agent is:

[0207] an anti-C5 monoclonal antibody (such as eculizumab or pexelizumab);

While Krause defines a C5a receptor-inactive therapeutic agent as an agent that does not satisfy the criteria set forth in paragraph [0035] for a C5a antagonist (see paragraph [0036]) and that a C5a receptor-inactive therapeutic agent can be "an active agent" (see paragraph [0037]).

[0035] A "C5a antagonist" or "C5a receptor antagonist" is any compound that exhibits C5a antagonist activity within the a C5a receptor-mediated chemotaxis, radioligand binding assay, or calcium mobilization assay as provided herein. In other words, in a calcium mobilization assay, a compound is a C5a antagonist if incubation of cells with 1 uM of C5a antagonist results in at least a 2-fold increase in the fluorescence response relative to that measured in the presence of C5a alone. In a chemotaxis assay, a compound is a C5a antagonist if it displays an affinity constant or IC₅₀ of 1 uM or less. Preferably, a C5a antagonist displays an IC₅₀ of less than 500 nM, 200 nM, 100 nM, 50 nM, 25 nM, 10 nM or 5 nM (in a chemotaxis and/or calcium mobilization assay) in a standard C5a receptor-mediated chemotaxis assay, radioligand binding assay, or calcium mobilization assay. In certain embodiments, C5a antagonists provided herein inhibit activation and/or activity of a primate C5a receptor, such as human C5a receptor, which may be a cloned, recombinantly expressed receptor or a naturally expressed receptor. For treating non-human animals of any particular species, a compound exhibiting high affinity for the C5a receptor of that particular species is preferred.

[0036] As used herein, "therapeutic agent" refers to a compound which has been shown to exhibit clinical efficacy in reducing the symptoms of one or more of arthritis (preferably rheumatoid arthritis) or another autoimmune disorder, asthma, cardio- or cerebrovascular disease, psoriasis, reperfusion injury, burns, or traumatic CNS or spinal cord injury. A "C5a receptor-inactive therapeutic agent" is such an agent that does not satisfy the criteria (above) for a C5a antagonist.

[0037] As used herein, "active agent" refers to either or both of the C5a antagonist and the C5a receptor-inactive therapeutic agent. This term is intended to encompass all salt, ester and prodrug forms of C5a antagonists and C5a receptor-inactive therapeutic agents, even where the prodrug is not active itself but is converted to the active form after administration to the patient.

All three pathways of complement activation (the classical, mannan-binding lectin and alternative pathway) lead to formation of C5 convertase, which cleave C5 into C5a and C5b.

C5a is a potent anaphylatoxin that mediates leukocyte chemotaxis, increases vascular permeability, alters smooth muscle tone and induces secondary inflammatory mediators.

C5a is a key regulator of inflammation, including attracting and activation circulating cells expressing C5aR, particularly monocytes, macrophages and neutrophils.

Given that C5 is common all pathways of complement activation, blockade at this point stops the progression of the cascade regardless of the stimuli. In addition, prevention of C5 cleavage effectively blocks the generation of the potent proinflammatory molecules C5a and the cell lytic terminal complement complex (TCC).

Note, too, that C5 blockade preserves the critical immunoprotective and immunoregulatory functions of upstream components that culminate in C3b-mediated opsonization and immune complex clearance.

The prior teachings of the anti-C5 antibody 5G1.1 or its recombinant forms (eculizumab or pexelizumab) served these purposes.

That Krause may classify the anti-C5 recombinant antibodies eculizumab or pexelizumab as C5a receptors inactive therapeutic agents does not detract for their potent anti-inflammatory activities at the time the invention was made to the ordinary artisan.

3. Priority.

Upon reconsideration of applicant's remarks, filed 01/25/2011, the effective filing date of the instant claims 1-11, 12-18, 45-50 and 59-60 appear to be the filing date of the priority application USSN 60/408,571, filed 09/06/2002.

Claims 20 and 51 do not appear to have an effective priority date back to priority application USSN 60/408,571, filed 09/06/2002.

4. Applicant's arguments in conjunction with the Wang declaration under 37 C.F.R. § 1.131 filed 01/25/2011 have been fully considered but are not found convincing essentially for the reasons of record.

Given applicant's arguments concerning the priority of the instant application to the provisional applications, that is, an effective filing date of 09/06/2002, applicant submits the withdrawal of the prior art rejection.

In contrast to applicant's / declarant's assertions, the Wang 131 declaration does not provide for the generic anti-C5 antibodies that inhibit the conversion of C5 into C5a and C5b, as currently claimed.

While the anti-C5 antibody BB5.1 described in the Wang 131 declaration may or may not inhibit the conversion of C5 into C5a and C5b,

there is no disclosure that the generic properties of anti-C5 antibodies that inhibit the conversion of C5 into C5a and C5b in the context of the claimed invention was described in a manner that provides for conception, diligence and reduction to practice prior to the claimed invention in a manner that obviates the prior art teachings.

Even if the anti-C5 antibody BB5.1 described in the Wang 131 declaration did inhibit the conversion of C5 into C5a and C5b,

it cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads.

See In re Smith 173 USPQ 679, 683 (CCPA 1972). See MPEP 2163.05(b).

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To provide a written description of the invention, the specification must include a written description of each and every element of the claimed subject matter.

See Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

See Ariad Pharmaceuticals Inc. v. Eli Lilly & Co., 94 USPQ2d 1161 (Fed. Cir. 2010).

A claim as a whole has only one effective filing date.

See Studiengesellschaft Kahle m.b.H. v. Shell Oil Co. 42 USPQ2d 1674, 1677 (Fed. Cir. 1997).

In turn and for the reasons herein /above, applicant's arguments in conjunction with the Wang declaration under 37 C.F.R. § 1.131 filed 01/25/2011 do not obviate the prior art teachings based upon Krause et al. (US 2004/0014782).

5. Upon reconsideration of applicant's amended claims, filed 01/25/2011, the previous objection to the claims has been withdrawn.

6. Upon reconsideration of applicant's amended claims, filed 01/25/2011, the previous rejections under 35 U.S.C. 112, second paragraph, have been withdrawn.

7. Upon reconsideration of applicant's amended claims, filed 01/25/2011, the previous rejection under 35 U.S.C. 112, first paragraph, enablement has been withdrawn.

8. Upon reconsideration of applicant's amended claims, filed 01/25/2011, the previous rejection under 35 U.S.C. 112, first paragraph, written description has been withdrawn.

9. Claims 1-11, 15-18, 20-21, 45-51 and 59-60 are rejected under 35 U.S.C. § 102(e) as being anticipated by Krause et al. (US 2004/0014782) (see entire document).

Applicant's arguments in conjunction with the Wang declaration under 37 C.F.R. § 1.131 filed 01/25/2011 have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that the C5a antagonists disclosed by Krause do not include anti-C5 antibodies and the reference does not disclose methods of kits including anti-C5 antibodies for use in treating respiratory disorders.

In contrast to applicant's narrow reading of Krause et al.,

Krause et al. is clearly drawn to C5a antagonists and compositions / kits comprising said C5a antagonists and their use to treat a variety of inflammatory or autoimmune diseases / conditions (e.g., Background, Summary of the Invention and Detailed Description of the Invention, including Terminology in paragraphs [0034]-[0039]).

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While applicant relies upon the disclosure of paragraphs [0206]-[0207] of Krause et al. to stand for the prior art anti-C5 antibodies to be C5a receptor-inactive therapeutic agents, the following is noted.

In contrast to applicant's assertions,

paragraph [0207] of Krause describes anti-C5 antibodies such as eculizumab or pexelizumab, which are the same anti-C5 antibodies recited in instant claim 49 and encompassed by anti-C5 antibodies that inhibit the conversion of C5 into C5a and C5b.

Eculizumab is the humanized version of the anti-C5 antibody, 5G1.1

Pexelizumab is the humanized single chain version of the anti-C5 antibody, 5G1.1.

[0206] Still other embodiments of the invention are directed to combinations in which at least one C5a receptor-inactive therapeutic agent is:

[0207] an anti-C5 monoclonal antibody (such as eculizumab or pexelizumab);

While Krause defines a C5a receptor-inactive therapeutic agent as an agent that does not satisfy the criteria set forth in paragraph [0035] for a C5a antagonist (see paragraph [0036]) and that a C5a receptor-inactive therapeutic agent can be "an active agent" (see paragraph [0037]).

[0035] A "C5a antagonist" or "C5a receptor antagonist" is any compound that exhibits C5a antagonist activity within the a C5a receptor-mediated chemotaxis, radioligand binding assay, or calcium mobilization assay as provided herein. In other words, in a calcium mobilization assay, a compound is a C5a antagonist if incubation of cells with 1 uM of C5a antagonist results in at least a 2-fold increase in the fluorescence response relative to that measured in the presence of C5a alone. In a chemotaxis assay, a compound is a C5a antagonist if it displays an affinity constant or IC₅₀ of 1 uM or less. Preferably, a C5a antagonist displays an IC₅₀ of less than 500 nM, 200 nM, 100 nM, 50 nM, 25 nM, 10 nM or 5 nM (in a chemotaxis and/or calcium mobilization assay) in a standard C5a receptor-mediated chemotaxis assay, radioligand binding assay, or calcium mobilization assay. In certain embodiments, C5a antagonists provided herein inhibit activation and/or activity of a primate C5a receptor, such as human C5a receptor, which may be a cloned, recombinantly expressed receptor or a naturally expressed receptor. For treating non-human animals of any particular species, a compound exhibiting high affinity for the C5a receptor of that particular species is preferred.

[0036] As used herein, "therapeutic agent" refers to a compound which has been shown to exhibit clinical efficacy in reducing the symptoms of one or more of arthritis (preferably rheumatoid arthritis) or another autoimmune disorder, asthma, cardio- or cerebrovascular disease, psoriasis, reperfusion injury, burns, or traumatic CNS or spinal cord injury. A "C5a receptor-inactive therapeutic agent" is such an agent that does not satisfy the criteria (above) for a C5a antagonist.

[0037] As used herein, "active agent" refers to either or both of the C5a antagonist and the C5a receptor-inactive therapeutic agent. This term is intended to encompass all salt, ester and prodrug forms of C5a antagonists and C5a receptor-inactive therapeutic agents, even where the prodrug is not active itself but is converted to the active form after administration to the patient.

All three pathways of complement activation (the classical, mannan-binding lectin and alternative pathway) lead to formation of C5 convertase, which cleave C5 into C5a and C5b.

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C5a is a potent anaphylatoxin that mediates leukocyte chemotaxis, increases vascular permeability, alters smooth muscle tone and induces secondary inflammatory mediators.

C5a is a key regulator of inflammation, including attracting and activating circulating cells expressing C5aR, particularly monocytes, macrophages and neutrophils.

Given that C5 is common to all pathways of complement activation, blockade at this point stops the progression of the cascade regardless of the stimuli. In addition, prevention of C5 cleavage effectively blocks the generation of the potent proinflammatory molecules C5a and the cell lytic terminal complement complex (TCC).

Note, too, that C5 blockade preserves the critical immunoprotective and immunoregulatory functions of upstream components that culminate in C3b-mediated opsonization and immune complex clearance.

The prior teachings of the anti-C5 antibody 5G1.1 or its recombinant forms (eculizumab or pexelizumab) served these purposes.

That Krause may classify the anti-C5 recombinant antibodies eculizumab or pexelizumab as C5a receptors inactive therapeutic agents does not detract for their potent anti-inflammatory activities nor their role as C5 antagonists at the time the invention was made to the ordinary artisan.

The following is reiterated for applicant's convenience.

Krause et al. teach the use of C5a antagonists, including anti-C5 antibodies (e.g., see paragraphs [0207] and [0277]) in the treatment of respiratory diseases, lung disorders, including ARDS and asthma (e.g., see paragraphs [0039], [0204], [0227], [0274]), including inhaled compositions, nebulizers or other devices for the treatment of asthma (e.g., see paragraphs [0273]—[0275], [0279]–[0281], [0288]–[0303]) as well as combinations for the treatment of lung disorders (e.g., see paragraphs [0200], [0226]–[0235]) and dosages consistent with the broad range (e.g., see paragraphs [0263]–[0300]) (see entire document).

Although the reference does not disclose that all of the properties or binding characteristics of antagonistic anti-C5 antibodies recited in the claims *per se* (e.g., reducing airway obstruction, reducing bronchial spasms, increasing airflow, inhibits the conversion of complement component C5 into C5a and C5b, etc.),

it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories, 58 USPQ2d 1508 (CAFC 2001). “{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable”. In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

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On this record, it is reasonable to conclude that the same patient is being administered the same active agent by the same mode of administration in the same amount in both the instant claims and the prior art reference. The fact that applicant may have discovered yet another beneficial effect from the method set forth in the prior art does not mean that they are entitled to receive a patent on that method.

Note that eculizumab or pexelizumab described in paragraphs [0207] is the same as 5G1.1, h5G1.1 or its single chain variant.

Applicant's arguments have not been found persuasive.

10. This is a New Grounds of Rejection.

Claims 1-11, 15-18, 20-21, 45-51 and 59-60 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Krause et al. (US 2004/0014782) (1449; #AE) in view of Evans et al. (U.S. Patent No. 6,355,245), Fung et al. (U.S. Patent No. 6,956,107), Fung et al. (U.S. Patent No. 6,998,468), Lobb et al. (U.S. Patent No. 5,871,734) (1449; #AA) and the known regimens of asthma therapy, as acknowledged on page 6, paragraph 2 of the specification.

Applicant's arguments in conjunction with the Wang declaration under 37 C.F.R. § 1.131 filed 01/25/2011 have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that the C5a antagonists disclosed by Krause do not include anti-C5 antibodies and the reference does not disclose methods of kits including anti-C5 antibodies for use in treating respiratory disorders.

In contrast to applicant's narrow reading of Krause et al., Krause et al. is clearly drawn to C5a antagonists and compositions / kits comprising said C5a antagonists and their use to treat a variety of inflammatory or autoimmune diseases / conditions (e.g., Background, Summary of the Invention and Detailed Description of the Invention, including Terminology in paragraphs [0034]-[0039]).

While applicant relies upon the disclosure of paragraphs [0206]-[0207] of Krause et al. to stand for the prior art anti-C5 antibodies to be C5a receptor-inactive therapeutic agents, the following is noted.

In contrast to applicant's assertions, paragraph [0207] of Krause describes anti-C5 antibodies such as eculizumab or pexelizumab, which are the same anti-C5 antibodies recited in instant claim 49 and encompassed by anti-C5 antibodies that inhibit the conversion of C5 into C5a and C5b.

Eculizumab is the humanized version of the anti-C5 antibody, 5G1.1

Pexelizumab is the humanized single chain version of the anti-C5 antibody, 5G1.1.

[0206] Still other embodiments of the invention are directed to combinations in which at least one C5a receptor-inactive therapeutic agent is:

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While Krause defines a C5a receptor-inactive therapeutic agent as an agent that does not satisfy the criteria set forth in paragraph [0035] for a C5a antagonist (see paragraph [0036]) and that a C5a receptor-inactive therapeutic agent can be "an active agent" (see paragraph [0037]).

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[0036] As used herein, "therapeutic agent" refers to a compound which has been shown to exhibit clinical efficacy in reducing the symptoms of one or more of arthritis (preferably rheumatoid arthritis) or another autoimmune disorder, asthma, cardio- or cerebrovascular disease, psoriasis, reperfusion injury, burns, or traumatic CNS or spinal cord injury. A "C5a receptor-inactive therapeutic agent" is such an agent that does not satisfy the criteria (above) for a C5a antagonist.

[0037] As used herein, "active agent" refers to either or both of the C5a antagonist and the C5a receptor-inactive therapeutic agent. This term is intended to encompass all salt, ester and prodrug forms of C5a antagonists and C5a receptor-inactive therapeutic agents, even where the prodrug is not active itself but is converted to the active form after administration to the patient.

All three pathways of complement activation (the classical, mannan-binding lectin and alternative pathway) lead to formation of C5 convertase, which cleave C5 into C5a and C5b.

C5a is a potent anaphylatoxin that mediates leukocyte chemotaxis, increases vascular permeability, alters smooth muscle tone and induces secondary inflammatory mediators.

C5a is a key regulator of inflammation, including attracting and activation circulating cells expressing C5aR, particularly monocytes, macrophages and neutrophils.

Given that C5 is common all pathways of complement activation, blockade at this point stops the progression of the cascade regardless of the stimuli. In addition, prevention of C5 cleavage effectively blocks the generation of the potent proinflammatory molecules C5a and the cell lytic terminal complement complex (TCC).

Note, too, that C5 blockade preserves the critical immunoprotective and immunoregulatory functions of upstream components that culminate in C3b-mediated opsonization and immune complex clearance.

The prior teachings of the anti-C5 antibody 5G1.1 or its recombinant forms (eculizumab or pexelizumab) served these purposes.

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That Krause may classify the anti-C5 recombinant antibodies eculizumab or pexelizumab as C5a receptors inactive therapeutic agents does not detract for their potent anti-inflammatory activities nor their role as C5 antagonists at the time the invention was made to the ordinary artisan.

Evans et al. (of record) provides the teachings of anti-C5 antibodies, including the 5G1.1 specificity, in the treatment of inflammatory diseases, including the specificities and advantages discussed herein above (e.g., see entire document, including Summary of the Invention; Background Physiology and Pathology, particularly as it reads on The Complement System; Description of the Preferred Embodiments; Favored Embodiments; and Examples)

The following references have been added to provide further evidence of targeting C5-mediated inflammation in the context of treating asthma at the time the invention was made.

Although Fung et al. (U.S. Patent No. 6,956,107) was focused on Factor D inhibitors,

Fung et al. teach the role of C5a anaphylatoxin in complement-mediated inflammation (e.g., see Background of the Invention), including the inhibition of C5a anaphylatoxin (e.g., see column 9, lines 39-41) in the context of severe asthma (e.g., see column 9, lines 62-63) as well as appropriate pharmaceutical formulations that can be administered by a variety of routes, including intranasal and intratracheal (e.g., see column 9, lines 32-38).

Although Fung et al. (U.S. Patent No. 6,998,468) was focused on complement Ca2 inhibitors,

Fung et al. teach the role of C5a anaphylatoxin in complement-mediated inflammation and the inhibition of the complement and lectin complement pathways including C5 convertases and C5 activation (e.g., see Background of the Invention and Applications of the Anti-C2a Molecules).

The following is reiterated for applicant's convenience.

Krause et al. teach the use of C5a antagonists, including anti-C5 antibodies (e.g., see paragraphs [0207] and [0277]) in the treat respiratory diseases lung disorders, including ARDS and asthma (e.g., see paragraphs [0039], [0204] [0227, [0274]), including compositions for the treatment of asthma (e.g., see paragraphs [0273]—[0275], [0279]–[0281], [0288]–[0303]) and instructions (e.g., see claim 29, paragraphs 263, [0273], [0278], [0297]) as well as combinations for the treatment of lung disorders (e.g., see paragraphs [0200], [0226]–[0235]) and dosages consistent with the broad range recited in claim 31 (e.g., see paragraphs [0263]–[0300]) (see entire document).

Although the reference does not disclose that all of the properties of functional or binding characteristics of antagonistic anti-C5 antibodies recited in the claims per se (e.g., reducing airway obstruction, reducing bronchial spasms, increasing airflow, inhibits the conversion of complement component C5 into C5a and C5b, etc.),

it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See *Bristol-Myers Squibb Company v. Ben Venue Laboratories* 58 USPQ2d 1508 (CAFC 2001). “{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable”. *In re Woodruff*, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). “The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. *In re Wiseman*, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in,

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or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Furthermore, the functional or binding characteristics of antagonistic anti-C5 antibodies recited in the claims (e.g., reducing airway obstruction, reducing bronchial spasms, increasing airflow, inhibits the conversion of complement component C5 into C5a and C5b, etc.) in the treatment of asthma or other pulmonary inflammatory conditions would have been obvious therapeutic endpoints in view of the teachings of the therapeutic utilities of the antagonistic anti-C5 antibodies taught by Krause et al., as these therapeutic endpoints would have been obvious therapeutic endpoints in the amelioration or treatment of said inflammatory pulmonary conditions.

In addition, Evans et al. provides for a more complete teachings of making and using 5G1.1 anti-C5 antibody in inhibiting inflammation, including the binding and functional characteristics recited in claims 12-16) (see entire document).

Note that eculizumab or pexelizumab described in paragraphs [0207] is the same as 5G1.1., h5G1.1.

In addition, page 6, paragraph 2 of the instant specification acknowledges the known reagents employed in asthma regimens.

Given the teachings of combination therapy by Krause et al., it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ antagonistic anti-C5 antibodies in combination with the known regimens either taught by Krause et al. or as acknowledged by page 6, paragraph 2 of the instant specification as equivalents or obvious substitutions regularly practiced by the ordinary artisan at the time the invention was made.

In addition to the teachings above, Lobb et al. teach that aqueous antibody solutions can be delivered to airways using a nebulizer (e.g., see column 6, lines 36-41 and column 12, lines 37-52) as well as the use of antibodies for the treatment of asthma (see entire document, including Summary of the Invention). Note, too, that Lobb et al. also teach the well known applicability of combination therapy, including combination having a therapeutic effect on airway responsiveness (e.g., see column 8, paragraphs 4-5).

On this record, it is reasonable to conclude that the same patients are being administered the same active agent by the same mode of administration in the same amount in both the instant claims and the prior art reference

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to employ combination therapy with anti-C5a antibodies in the treatment of certain respiratory / lung disorders / diseases such as asthma. One would have been motivated with a reasonable expectation of success to administer the antibodies directly to the respiratory mucosa, which is often the first line of encounter of an immune system with pathogenic organisms and by the teachings of the prior art as a known and effective means to target the respiratory system in the treatment of certain disorders/diseases.

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

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An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See *KSR Int'l Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Given that the prior art goal was to inhibit complement activation in order to treat pulmonary diseases/conditions, incorporating known inhibitors such as anti-C5 antibodies into therapeutic regimens to treat inflammatory lung / pulmonary conditions such as asthma would have been routine to the ordinary artisan at the time the invention was made and therefore obvious in designing therapeutic regimens to treat such inflammatory pulmonary diseases / conditions.

From the teachings of the references, a person of ordinary skill in the art would have a reasonable expectation of success at the time the invention was made. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments have not been found persuasive.

11. Claims 1-11, 15-18, 20-21, 45-51 and 59-60 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 31-45 and 48 of copending USSN 11/127,438.

The instant and copending claims are drawn to the same or nearly the same methods of treating pulmonary conditions such as asthma with the same anti-C5 antibodies. Combination therapy in the treatment of various conditions, including pulmonary conditions / asthma were well known in the prior art at the time the invention was made.

The instant and copending claims either anticipate or render obvious one another.

Applicant's request, filed 01/25/2011, that this rejection be held in abeyance until otherwise allowable subject matter is identified in the instant application is acknowledged.

The rejection is maintained for the reasons of record.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phillip Gambel/
Primary Examiner
Technology Center 1600
Art Unit 1644
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